CLAIMS

1. An isolated binding pocket of a SCF complex or component thereof associated with substrate selection and/or orientation.

2. An isolated binding pocket of claim 1 wherein the component is an F-box protein comprising an F-box and a WD repeat domain.

3. Molecules or molecular complexes that comprise all or parts of one or more of a binding pocket as claimed in claim 1, or a homolog of the binding pocket that has similar structure and shape.

4. A crystal comprising a binding pocket of an F-box protein involved in substrate selection and/or orientation.

5. A crystal of claim 4 wherein the F box protein comprises an F box and a WD repeat domain.

6. A crystal comprising a binding pocket of claim 1 complexed or associated with a substrate.

7. A crystal of claim 6 wherein the ligand or substrate is a CPD motif containing protein, or part thereof.

8. A crystal according to claim 4 having the structural coordinates shown in Table 6.

9. A model of a binding pocket of a SCF complex using a crystal according to claim 8.

10. A model of: (a) a binding pocket of an SCF complex of claim 1; and (b) a modification of the model of (a).

11. A model of a binding pocket of an F-box protein of claim 2 that substantially represents the structural coordinates specified in Table 6.

12. A binding pocket of claim 2 which comprises a WD40 repeat domain characterized by one or more of the following characteristics:

    (a) a 7 or 8 blade β-propeller structure, in particular a 8 blade β-propeller structure;

    (b) a disk like structure characterized by a cavity in the middle and two opposing circular surfaces of different size;

    (c) a conical frustum of about 40Å top surface and about 50Å bottom surface, an overall thickness of 30Å and a central pore of 6Å diameter; and

    (d) a CPD binding site on the top surface of the frustum of (c) and running across the edge, while the bottom surface of the frustum links to the F-box domain.

13. A binding pocket of claim 2 which is characterized by one or more of the following characteristics:

    (i) a pThr-Pro binding pocket;

    (ii) a deep hydrophobic pocket that selects hydrophobic residues N-terminal to the phosphorylation site of a CPD motif, and

    (iii) a through space electrostatic selection against basic residues C-terminal to the phosphorylation site of a CPD motif.

14. A binding pocket of claim 2 which comprises a helical linker characterized by α helices that form a stalk and pedestal like structure that connects and orients a WD repeat domain.

15. A binding pocket of claim 2 as shown in Figure 3a which is further characterized by one or more of the following:

(a) a αhelix that is 30Å in length and is anchored at its N-terminus to the hydrophobic core of an F-box/helical extension and at its C-terminus to the hydrophobic core of a WD repeat domain,

(b) the helix of (a) anchored at its amino terminus to an F-box through hydrophobic interactions;

(c) a second αhelix packed along the base of the helix of (a) or (b) opposite to the F-box through hydrophobic interactions; and

(d) a C-terminal end of the helix of (a) inserted obliquely between propeller blades β7 and β8 of an WD40 domain through van der Wals and hydrophobic interactions.

16. A binding pocket of claim 2 which is a CPD motif binding pocket comprising a hydrophobic pocket that surrounds the open central channel of a 7 or 8 blade WD repeat propeller.

17. A binding pocket of claim 2 which is a Cdc4 polypeptide that interacts with a CPD motif characterized by one or more of the following:

(a) a WD repeat domain surface composed of invariant and highly conserved residues from β-propeller blades;

(b) a three-sided pocket formed by Trp426, Thr386, and Arg 485;

(c) a three-sided pocket formed by Trp426, Thr441, Thr 465, and Arg 485;

(d) a hydrophobic pocket composed of Trp 426, Trp 717, Thr 386, and Val 384,

(e) a pocket formed by Leu634, Met590, and Tyr574; and

(f) a pocket formed by Arg485, Arg467, Arg534, Tyr548, and Arg572.

18. A binding pocket of claim 1 comprising one or more of the amino acid residues for an F-box protein crystal or F-box protein –substrate crystal identified in Table 3 or Table 4.

19. A computer-readable medium having stored thereon a crystal of claim 8.

20. A method of determining the secondary and/or tertiary structures of a polypeptide comprising the step of using a crystal of claim 8.

21. A method of screening for a ligand capable of associating with a binding pocket and/or inhibiting or enhancing the atomic contacts of interactions in a binding pocket, comprising the use of a crystal of claim 8.

22. A method of conducting a drug discovery business comprising:

(a) providing one or more systems employing the atomic interactions, atomic contacts, or structural coordinates of a binding pocket of claim 1, to identify agents by their ability to inhibit or potentiate the atomic interactions or atomic contacts of the binding pocket;

(b) conducting therapeutic profiling of agents identified in step (a), or further analogs thereof, for efficacy and toxicity in animals; and

(d) formulating a pharmaceutical preparation including one or more agents identified in step (b) as having an acceptable therapeutic profile.

23. A method for regulating an SCF complex by changing a structure of a binding pocket of claim 1.

24. Use of a modulator of a binding pocket of claim 1 in the manufacture of a medicament to treat and/or prevent a disease in a mammalian patient.

25. A pharmaceutical composition comprising a ligand or modulator of a binding pocket according to claim 1, and optionally a pharmaceutically acceptable carrier, diluent, excipient or adjuvant or any combination thereof.